

Application No.: 10/506,693

Attorney Docket No.: 47675-86

First Applicant's Name: Kurt Berlin

Application Filing Date: 21 April 2005

Notice of Non-Compliant Amendment Dated: 19 June 2009

Date of Response: 24 June 2009

Examiner: Katherine D. Salmon

IN THE CLAIMS:

Applicants, pursuant to 37 C.F.R. § 1.121, submit the following amendments to the claims:

1. (Currently amended) A method for detecting the presence of a cancer disease characterized by an increased amount of organ-specific free floating DNA, comprising:

obtaining a bodily fluid sample from a test human;

measuringdetermining an amount or presence of free floating DNA that originates from a particular organ in the sample comprising analysing for a DNA methylation pattern that is characteristic for the particular organ; and

determining the presence of a disease characterized by an increased amount of organ-specific free floating DNA based on comparing the measured amount or presence of free floating DNA that originates from the particular organ of the test human[.] with that of a normal control value, and determining the presence of a cancer characterized by an increased amount of organ-specific free floating DNA based on an increased measured amount of organ-specific free floating DNA.

2. (Currently amended) A method for detecting the presence of a cancer disease characterized by an increased amount of organ-specific free floating DNA, comprising:

obtaining a bodily fluid sample from a test human;

measuringdetermining an amount of total free floating DNA in the sample;

measuringdetermining an amount of free floating DNA that originates from a particular organ in the sample comprising analysing for a DNA methylation pattern that is characteristic for the organ; and

determining the presence of a disease characterized by an increased amount of organ-specific free floating DNA based on comparing the total measured amount of free floating DNA and the fraction of free floating DNA that originates from the organ of the test human, with that of a normal control value, and determining the presence of a cancer characterized by an increased

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amount of organ-specific free floating DNA based on an increased fraction of organ-specific free floating DNA.

3. (Previously presented) The method of any one of claims 1 and 2, wherein the sample is treated before the amount or presence of free floating DNA is determined.

4. (Previously presented) The method of claim 3, wherein the sample is treated by at least one centrifugation, filtering, heating, cooling, concentration and chemical treatment.

5. (Cancelled)

6. (Currently amended) The method of any one of claims 1 and 2, wherein the methylation pattern is characteristic for the particular organ and not found in other organs involved in the cancerdisease characterized by an increased amount of organ-specific free floating DNA of interest.

7. (Cancelled)

8. (Previously presented) The method of any one of claims 1 and 2, wherein the sample comprises at least one bodily fluid selected from the group consisting of whole blood, blood plasma, blood serum, urine, sputum, ejaculate, semen, tears, sweat, saliva, lymph fluid, bronchial lavage, pleural effusion, peritoneal fluid, meningeal fluid, amniotic fluid, glandular fluid, fine needle aspirates, nipple aspirate fluid, spinal fluid, conjunctival fluid, vaginal fluid, duodenal juice, pancreatic juice, bile and cerebrospinal fluid.

9. (Previously presented) The method of any one of claims 1 and 2, wherein determining the methylation pattern comprises subjecting the DNA to a chemical or enzymatic treatment that converts all unmethylated cytosines in the DNA into uracil but leaves position 5-

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methylated cytosines unmodified.

10. (Currently amended) A method for detecting the presence of a cancer~~disease~~ characterized by an increased amount of organ-specific free floating DNA, comprising:

obtaining a bodily fluid sample from a test human;

measuring~~determining~~ an amount or presence of free floating DNA that exhibits a DNA methylation pattern characteristic of a particular organ;

determining, based on the measuring, whether there is an increased level, relative to that of a control value, of free floating DNA that originates from the organ; and

determining, based on finding an increased level of free floating DNA that originates from the organ of the test human, a presence of a cancer~~disease~~ characterized by an increased amount of organ-specific free floating DNA ~~based on comparing the presence of such an increased level of free floating DNA that originates from the organ of the test human, with that of a normal control value.~~

11. (Currently amended) A method for detecting the presence of a cancer~~disease~~ characterized by an increased amount of organ-specific free floating DNA, comprising:

obtaining a bodily fluid sample from a test human;

measuring~~determining~~ an amount of total free floating DNA in the sample;

measuring~~determining~~ an amount of free floating DNA that originates from a specific organ by determining an amount of free floating DNA that exhibits a DNA methylation pattern characteristic of the organ;

determining the fraction of total free floating DNA that originates from the specific organ;

determining whether an increased fraction, relative to that of a normal control value level of free floating DNA that originates from the specific tissue, cell type or organ is present; and

determining, based on finding an increased fraction of free floating DNA that originates from the organ of the test human, the presence of a cancer~~disease~~ characterized by an increased amount of organ-specific free floating DNA, ~~based on comparing the presence of such an increased~~

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~~level of free floating DNA that originates from the organ of the test human, with that of a normal control value.~~

12. (Previously presented) A method for determining the fraction of total free floating DNA in a bodily fluid that originates from a specific organ, comprising:

obtaining a bodily fluid sample of a test human;

conditioning the sample to provide for binding of total free floating DNA to a surface;

binding an amount of the total free floating DNA to the surface;

detecting an amount of total free floating DNA by measuring the amount of DNA bound to the surface;

subjecting the surface comprising the bound DNA to at least one of a chemical and enzymatic treatment that converts all unmethylated cytosines in the DNA into uracil but leaves position-5 methylated cytosines unmodified;

amplifying the treated DNA;

analysing several methylation-specific positions in the treated DNA, and thereby determining an amount of DNA that exhibits an organ-specific DNA methylation pattern; and

comparing the amount of DNA that exhibits an organ-specific DNA methylation pattern to the amount of detected total free floating DNA, thereby determining the fraction of free floating DNA that originates from the specific organ in the total free floating DNA.

13. (Currently amended) The method of claim 12, further comprising:

determining whether an increased level of free floating DNA that originates from the specific organ is present; and

determining the presence of a ~~cancer~~ disease characterized by an increased amount of organ-specific free floating DNA, based on comparing the presence of such an increased level of free floating DNA that originates from the organ of the test human, with that of a normal control value.

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14. (Previously presented) The method of any one of claims 1, 2, 10, 11, 12 and 13, wherein measuring the total amount of free floating DNA comprises use of at least one means selected from the group consisting of: intercalating fluorescent dyes or other dyes exhibiting changing fluorescence properties upon binding to DNA; hybridisation to DNA specific oligonucleotide or PNA oligomer probes; real time PCR assays; real time amplification procedures; UV-Vis absorbance; and amplification procedures with subsequent determination of the amount of product amplicate formed.

15. (Cancelled)

16. (Cancelled)